WEST Search History

DATE: Tuesday, July 02, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L19	L18 and cationic	14	L19
L18	L17 and biopolymer	57	L18
L17	(antibacterial or anti-bacterial or antimicrobial or anti-microbial or antibiotic or anti-biotic) and l15	2160	L17
L16	L15 and l12	2	L16
L15	absorption with enhanc$4	13575	L15
L14	absorption same enhanc$4	20398	L14
L13	carrageenan and ceftriaxone and capmul and calcium	2	L13
L12	l10 same l9	8	L12
L11	L10 and l9	13	L11
L10	biopolymer same (antibacterial or anti-bacterial or antimicrobial or anti-microbial or antibiotic or anti-biotic)	122	L10
L9	biopolymer same cationic	258	L9
L8	L6 and l5	70	L8
L7	L6 and l2	433	L7
L6	L2 and (antibacterial or anti-bacterial or antimicrobial or anti-microbial or antibiotic or anti-biotic)	433	L6
L5	L2 and biopolymer same cationic	258	L5
L4	L2 and biopolymer same cationic	258	L4
L3	L2 biopolymer same cationic	1216	L3
L2	L1 and cationic	1216	L2
L1	biopolymer	7636	L1

END OF SEARCH HISTORY

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L19: Entry 12 of 14 File: USPT Nov 9, 1999

DOCUMENT-IDENTIFIER: US 5981474 A
TITLE: Solubilization of pharmaceutical substances in an organic solvent and preparation of pharmaceutical powders using the same

Detailed Description Paragraph Right (3):
To assist in the understanding of the present invention, but not to be bound by theory, it is believed that the pharmaceutical substance and the amphiphilic material are associated in the form of a complex between the amphiphilic material and the pharmaceutical substance, with the complex being substantially not soluble in aqueous liquids at a physiological pH. Preferably, the amphiphilic material and the pharmaceutical substance have oppositely charged ionic portions which associate to form an ion pair complex. Such an ion pair complex is referred to as a hydrophobic ion pair (HIP) complex. Preferably, the pharmaceutical substance comprises a cationic portion which associates with an anionic portion of the amphiphilic material.

Detailed Description Paragraph Right (4):
The pharmaceutical substance may be any substance which may be administered to a human or animal host for a medical purpose, which is normally a curative or therapeutic purpose. The pharmaceutical substance is preferably directly soluble to some meaningful degree in an aqueous liquid at a physiological pH. As used herein, a physiological pH is a pH of from about 1 to about 8. Preferably, the pharmaceutical substance exhibits a charged character when dissolved in an aqueous liquid at a physiological pH and more preferably exhibits a positively charged, or cationic, character. As used herein, a pharmaceutical substance includes various salt forms of a substance as well as ionic forms and dissociation products, such as may be found in an aqueous solution.

Detailed Description Paragraph Right (5):
The pharmaceutical substance may comprise a protein or other polypeptide, an analgesic or another material. The following is a non-limiting list of representative types of pharmaceutical substances which may be used with the present invention, with a few specific examples listed for each type of pharmaceutical substance: cholinergic agonists (pilocarpine, metoclapramide); anticholinesterase agents (neostigmine, physostigmine); antimuscarinic drugs (atropine, scopalamine); antidrenergics (tolazoline, phentolamine, propranolol, atenolol); ganglionic stimulating agents (nicotine, trimethaphan); neuromuscular blocking agents (gallamine, succinylcholine); local anesthetics (procaine, lidocaine, cocaine); benzodiazepines (triazolam); antipsychotics (chlorpromazine, triflupromazine, imipramine, amitriptyline, phenelzine); antiparkinson's drugs (L-dopa, dopamine); opioids (morphine, naloxone, naltrexone, methadone); CNS stimulants (theophylline, strychnine); autocoids (histamine, betazole, chlorpheniramine, cimetedine); anti-inflammatories (tolmetin, piroxicam); anti-hypertensives (clonidine, hydralazine, minoxidil); diuretics (metalozone, bumetamide); polypeptides (lysopressin, vasopressin, oxytocin, insulin, calcitonin, gene-related peptide, LHRH agonists, ACTH, growth hormone); antifungals (clotrimazole, miconazole); antimalarials (chloroquine, primaquine); antiprotozoals (pentamidine, melarsoprol); antihelminthics (piperazine, oxamniquine); antimicrobials (streptomycin, erythromycin, cefaclor, ceftriaxone, oxytetracycline, rifampicin, isoniazid, dapsone); aminoglycosides (gentamycin, neomycin, streptomycin); antineoplastics (mechlorethamine, melphalan, doxorubicin, cisplatin); and anticoagulants (heparin). Additionally, the pharmaceutical substance may be a sympathomimetic drug such as catecholamines (epinephrine, norepinephrine); noncatecholamines (amphetamine, phenylephrine); and .beta..sub.2 -adrenergics (terbutaline, albuterol).

Detailed Description Paragraph Right (8):
Examples of anionic amphiphilic materials include sulfates, sulfonates, phosphates (including phospholipids), carboxylates, and sulfosuccinates. Some specific anionic amphiphilic materials useful with the present invention include: sodium dodecyl sulfate (SDS), bis-(2-ethylhexyl) sodium sulfosuccinate (AOT), cholesterol sulfate and sodium laurate. Examples of cationic amphiphilic materials include those having an ammonium

group or a guadinium group, including substituted variations of those groups. Specific cationic amphiphilic materials include cetyltrimethylammonium bromide and cetyltrimethylammonium chloride. Preferred amphiphilic materials are those posing little or substantially no toxicological problem for the human or animal host. Particularly preferred anionic amphiphilic materials are SDS and AOT.

Detailed Description Paragraph Right (28):
As used in the present invention, the term "anionic detergents" encompasses any hydrophobic material that is a salt of an acid which can be employed to modify solubility properties in the described way, including sulfates, sulfonates, phosphates, and carboxylates. Sulfates are the salts of the stronger acids in this series and, therefore, the most efficient at forming ion pairs. Provided that the alkyl chains or aryl rings are of 8-18 carbons in length, they are potential candidates for HIP methodology. Presumably cationic detergents, such as dodecylamine hydrochloride or cetyltrimethylammonium bromide (CTAB), may also work for negatively charged polypeptides.

Detailed Description Paragraph Right (88):
The administration of HIP complexes to a patient may be accomplished in a number of ways. A biodegradable polymer/HIP complex system may be dissolved in an organic solvent, for example N-methyl pyrrolidone, and injected subcutaneously to form an implant, processed to form microspheres which can be injected subcutaneously or intramuscularly, processed to form an implant which is placed surgically under the skin, or given orally as part of an oral delivery system for peptides and proteins. The solid HIP complex may also be prepared as a suspension or a non-aqueous solution, which may be injected or placed on the skin where the complex may partition into the skin. The HIP complex may also be nebulized and administered to a patient via inhalation, for pulmonary drug delivery. The HIP complex may also be formulated to be given orally, such that it is protected from degradation in the stomach via an enterically coated capsule, and released in either the upper or lower intestinal tract. The HIP complex may be loaded alone or in conjunction with oils, bile salts, or other enhancers to increase absorption. The HIP complex may also be suspended or dissolved in oil and introduced to the patient as a rectal or vaginal suppository.

Other Reference Publication (7):
Powers et al., "Enhanced Solubility of Proteins and Peptides in Nonpolar Solvents Through Hydrophobic Ion Pairing," Biopolymers, vol. 33 (1993), pp. 927-932, John Wiley & Sons, Inc.

Other Reference Publication (12):
Meyer et al., "Solution Behaviour of a-Chymotrypsin Dissolved in Nonpolar Organic Solvents Via Hydrophobic Ion Pairing," Biopolymers, vol. 35 (1995) pp. 451-456, John Wiley & Sons, Inc.